REMARKS

By this amendment, claims 1-28 and 30-40 have been canceled without prejudice and without disclaimer of the subject matter contained therein. Applicants hereby reserve the right to pursue the canceled matter in one or more continuing or divisional applications. Several claims have been amended, and new claims 57-61 have been added. No new matter has been introduced. Claims 29, and 41-61 are now pending.

This Amendment and Response is being filed contemporaneously with an Information Disclosure Statement, and a Request for Corrected Inventorship. The Request for Correction of Inventorship deletes prior inventors Huong T. Dang and Kevin P. Lowitz, due to claim amendments.

Election/Restriction

Applicant notes with appreciation the examiner's acknowledgement of the election of Group XXII, and official treatment of amended claim 29 and claims 41-56 added in the response to the restriction requirement.

Claim Rejections

35 U.S.C. § 112, second paragraph

Claims 29, 41-43, and 46-56 stand rejected for allegedly being indefinite. Specifically, the action queries what activity is related to sensorimotor processing or arousal in the thalamus. Applicant notes that, as clearly indicated on page 19 and in Table E (and supporting text) of the specification, proteins located or expressed in areas of the thalamus are associated with sensorimotor processing and arousal and disorders thereof. Accordingly, the activity of those proteins is related to sensorimotor processing and arousal. Applicants have amended the claims to remove the use of the term "activity" to avoid any confusion. The action further queries what is being activated. Because the RUP35 receptor exhibits a detectable level of constitutive activity, as shown in Figure 2, whereby it increases intracellular IP3, Applicants have amended the claims to remove the use of the term "activation" to avoid any confusion. Thus, the rejection is moot. Withdrawal of the rejection is respectfully requested.

35 U.S.C. §§ 101, 112, first paragraph

The action sets forth a number of theories for rejecting the claims for alleged lack of utility under 35 U.S.C. § 101[1] and, accordingly, for lack of enablement under 35 U.S.C. § 112, first paragraph.

I. The Specification Provides a Specific, Substantial and Credible Utility

Applicants respectfully assert that the specification provides specific, substantial and credible utility as required under 35 U.S.C. § 101.

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[1] In one of these theories, the Office Action appears to dismiss the instant application's utility claim for RUP35, in part, on the basis that 1) RUP35 is an orphan receptor; 2) function of an orphan GPCR can not be determined by homology to other GPCRs, and 3) Watson et al. pages 223-230 teaches that knowledge of a GPCR's function is not possible for an orphan receptor due to the fact that the receptor's natural ligand is by definition not known. While RUP35 is, and was at the time of filing, an orphan receptor, this argument is completely without merit. Applicants need not rely on homology to establish the function of RUP34, other than to further establish that it is a GPCR. Rather, Applicants are relying upon expression data to establish RUP35's utility. Watson et al. pages 223 to 230 does NOT teach that a natural ligand is necessary to reliably predict the function of an orphan GPCR. Applicants fail to see how these pages could possibly be interpreted in this manner. Even if Watson were to make this argument, he would be ***wrong***. Knowledge of a GPCR's natural ligand ***is simply not necessary*** for establishing the function for such a receptor. In fact, it is possible to know a receptor's function and develop and market pharmaceutical agents targeting it without any understanding of the natural ligand which activates the receptor. For instance, the agonists of the so-called niacin receptor have long been recognized and used to raise HDL levels in man, e.g. nicotinic acid and acipomox. The natural ligand for this receptor is still a mystery. (Karpe and Frayn Lancet. 2004 Jun 5; 363(9424):1892-4; see IDS Ref. CQ). Similarly, many opiates were identified and developed and the analgesic functionality of the mu-opiate receptor was appreciated long before the first endogenous agonists of that receptor were discovered in 1975 (Zadina et al. Ann N Y Acad Sci. 1999; 897:136-44; see IDS Ref. CV). Applicants may very likely develop and market modulators of RUP35 without ever knowing the natural ligand. It remains unclear to Applicant how knowledge of a receptor's natural ligand is a prerequisite to a finding of utility when such knowledge is not necessary to convince the FDA of the function of a drug which modulates the receptor, and is not necessary to treat real live human beings. The fact that such knowledge is not required by the FDA is highly indicative that real world uses exist even where the natural ligand is unknown. Applicants note, however, that this entire line of reasoning is moot, since, for the reasons set forth in this response, the present application satisfies the utility requirement by asserting a specific, substantial, and credible utility.

The specification clearly asserts methods for treating thalamus-related disorders and for direct identification of agonists or inverse agonists applicable as therapeutic agents (see spec., p. 1-2) in treating thalamus-related disorders (see spec., p.19, Table E) and in particular those related to sensorimotor processing or arousal (see spec., p. 53). Those of skill in the art, at the time of filing, would have recognized sensorimotor processing disorders include tremor disorders, action tremor disorders, and disorders of impaired motor coordination, and that arousal disorders include impaired cognitive performance. See, Goodman & Gilman's The Pharmacological Basis of Therapeutics (1996) 9th Edition, McGraw-Hill, p. 465, IDS reference CR; Elble (1998) Movement Disorders, 13:35-39, IDS reference CO; Portas et al. (1998) The Journal of Neuroscience, 18:8979-8989, IDS reference CS; and Jeljeli et al. (2000) Neuroscience Research, 38:155-164, IDS reference CP. Thus, the specification clearly asserts a specific and substantial utility, as discussed further below.

A. The Utility is Specific

The asserted utility, that RUP35 can be used in treating thalamus-related disorders and for direct identification of therapeutic agents therefor, is specific in that each of the claims is directed to a specific receptor (RUP35), and not to G Protein-Coupled Receptors (GPCRs) generally, or another receptor group. Further, the asserted utility is specific to thalamus-related disorders, particularly those related to sensorimotor processing and/or arousal. Thus, the asserted utility is specific with respect to RUP35 and the disorder to be treated.

B. The Utility is Substantial

The use of RUP35 in treating, or screening candidate compounds for treating thalamus-related disorders is a real-world use. Substantial utility is found where the candidate compound, itself has specific and substantial utility. To have specific and substantial utility, there must be a real-world use for treatment of a specified disease. Here, it is clear that the disease is a disorder associated with the thalamus, particularly sensorimotor processing disorders and/or arousal disorders. Such disorders are well-known in the art and include tremor disorders, action tremor disorders, disorders of impaired motor coordination, and impaired cognitive performance, as noted above. Thus, the specification teaches a substantial, real-world utility.

C. The Revised Interim Utility Guidelines Support Applicant's Assertion of Utility

Each of Applicants' assertions above with regard to the utility of the present invention is supported by the Revised Interim Utility Guidelines Training Materials (available at http://www.uspto.gov/web/menu/utility.pdf). Example 12 of the Revised Interim Utility Guidelines Training Materials is directed to Receptors. (See Annex 1.) Claim 1 of Example 12 recites "Isolated receptor A", and Claim 2 of Example 12 recites a method of identifying materials which bind to receptor A.

In the Example, one utility for the receptor of Claim 1 is the method of identifying materials which bind to receptor A, as recited in Claim 2 of the Example. For both Claim 1 and Claim 2 of the Example, the guidelines conclude that a specific utility has been asserted, because the method of identifying materials which bind to a specific receptor, namely receptor A, is a method that is not applicable to the general class of receptors. This is similar to the present case, where Applicants' asserted utility is specific to the RUP35 receptor (SEQ ID NO.:16). Thus, under the guidelines, Applicants have clearly asserted a specific utility.

With regard to the question of substantial utility, the example notes it must be determined whether the material binding to receptor A has a specific and substantial utility. In the Example, the utility for the materials identified is as a therapeutic exercising control over receptor A. Because there is no expression data, or any disclosure of any disease or condition associated with receptor A, the Example concludes that the method of treating the unspecified, undisclosed disease or condition does not define a "real world" context of use. However, ***in sharp contrast to the Example***, Applicants have ***clearly and specifically*** associated RUP35 with the thalamus, and, more particularly, sensorimotor processing and arousal disorders. Thus, unlike the Example, there is a specific and disclosed disease or condition associated with the receptor, leading to a "real world" context of use. Accordingly, under the guidelines, Applicants' asserted utility is substantial.

D. The Utility is Credible

The action provides no evidence to contest the credibility of the asserted utility. Accordingly, the asserted utility is specific, substantial, and credible.

E. RUP35 would have been recognized as a GPCR

The Action questions whether RUP35 is a GPCR on page 6, lines 5-6 and then later indicates that "The hRUP35 of instant invention is considered by the examiner to be a member of the orphan receptor of G-protein coupled receptors." Applicant notes for the record that although it is clear from the specification and the discussion herein that RUP35 was known to be a GPCR at least at the time of filing, Applicant does not rely solely on RUP35's status as a GPCR for utility purposes.

It is clear from the specification and claims as originally filed, that RUP35 is a GPCR. References to GPCRs are found throughout the specification, claims, and even in the title. In almost every instance throughout the specification, RUP35 is specifically referred to as a GPCR or is referred to in a section discussing GPCRs, where RUP35 is discussed along with other GPCRs. Similarly, RUP35 is listed in several tables identifying other GPCRs. For example, hRUP35 appears in Table C under the heading "Disclosed Human Orphan GPCRs" and is discussed in Example 1 entitled "Endogenous Human GPCRs." There is no suggestion that RUP35 is anything other than a GPCR anywhere in the specification or claims. Indeed, original claim 29, setting forth a claim to RUP35 states "29. A ***G protein-coupled receptor*** encoded by an amino acid sequence of SEQ.ID.NO.:16." There can be no doubt that the specification teaches RUP35 is a GPCR.

It would be readily apparent to a person skilled in the art from the technical knowledge available when the application was filed that hRUP35 is a G protein-coupled receptor (GPCR). It was well known to the skilled artisan that GPCRs are characterized by seven transmembrane (membrane spanning) domains, designated TM-1 to TM-7 [*see, e.g.,* page 1, right column, paragraph [0005] of the application as filed; and page 2, left column, lines 13-27, Figure 2, and Figure 3 of Probst et al. (1992) DNA Cell Biol., 11:1-20, See IDS reference CT]. It was well known to the skilled artisan that TM-6 is characterized by a tryptophan residue and a proline residue conserved in many GPCRs (*see, e.g.,* page 10, lines 2-4 of the application as filed; and page 2, left column, lines 32-40, to right column, lines 1-5, Figure 2, and Figure 3 of Probst et al.). It was well known to the skilled artisan that GPCRs are characterized by a highly conserved arginine residue at the intracellular end of TM3, frequently as part of a "DRY" motif (*see, e.g.,* page 12, left column, lines 30-34, Figure 2, and Figure 3 of Probst et al.)

Methods of predicting the location of the transmembrane domains of a GPCR based on the sequence were available at the priority date of the application. One such method is TMHMM (transmembrane hidden Markov model), which is described in Sonnhammer et al. (1998) In J Glasgow et al, eds, Proc Sixth Int. Conf. on Intelligent Systems for Molecular Biology, 175-182, See IDS reference CU. In order to demonstrate to the Examiner that known methods could have been applied by the skilled person to identify TM-1 to TM-7, the conserved tryptophan and proline residues in TM-6, and the highly conserved arginine residue at the intracellular end of TM3, Applicants have applied the TMHMM method to SEQ ID NO:16 (RUP35 amino acid sequence). The result is shown in **Annex 2**.

Annex 2 shows that hRUP35 is predicted to have seven transmembrane regions, as expected for a GPCR. **Annex 2** shows that TM-6 is predicted to correspond to amino acids 228-250 of SEQ ID NO:16. This predicted amino acid sequence for TM-6, shown in **Annex 3**, contains a tryptophan residue (amino acid position 241) and a proline residue (amino acid position 243), consistent with the tryptophan and proline residues which are conserved in TM-6 of many GPCRs. The highly conserved arginine residue at the intracellular end of TM3 can be found at amino acid position 126, as part of a DRY motif.

Also note that elevation of a level of intracellular IP3 by RUP35 is consistent with RUP35 being a G protein-coupled receptor (*see*, e.g., the Table on pages 19 to 20).

It follows that it would be readily apparent to a person skilled in the art from the technical knowledge available when the application was filed that hRUP35 is a GPCR, particularly in light of the teachings found in the specification.

35 U.S.C. § 112, First paragraph

The claims were also rejected under 35 U.S.C. § 112, first paragraph, simply because they were rejected under 35 U.S.C. § 101. As discussed above, Applicants respectfully assert that the 35 U.S.C. § 101 rejections should be withdrawn, and likewise respectfully request that the rejection under 35 U.S.C. § 112, first paragraph be withdrawn as well.

Additionally, claims 44-56 were rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking written description support. Claim 44 has been amended to point out that the primers of SEQ.ID.NOs.:41 and 42 are specific primers and the PCR process is RT-PCR. Additional claims have been added to claim related features and more particularly set forth the

RT-PCR process used. Applicant respectfully asserts that the recited PCR conditions specifically amplify RUP35 nucleic acid sequence from human cDNA in RT-PCR.

Applicants respectfully assert that they have fully responded to each outstanding rejection and objection.

Each of the references cited herein is being submitted in an Information Disclosure Statement filed contemporaneously herewith for entry into the official file.

Although Applicants believe no fee is due, the Commissioner is hereby authorized to debit any fee due or credit any overpayment to Deposit Account 50-1275.

Early reconsideration and allowance of all pending claims is respectfully requested. The examiner is requested to contact the undersigned attorney if an interview, telephonic or personal, would facilitate allowance of the claims.

Respectfully submitted,

COZEN O'CONNOR

Date: May 10, 2005

by: Michael A. Patané
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ANNEX 1

Excerpted from the **REVISED INTERIM UTILITY GUIDELINES TRAINING MATERIALS**

Example 12: Receptors

Specification: The specification discloses a protein, isolated from a cell membrane preparation, which is the binding partner for protein X. The specification does not characterize the isolated protein with regard to its biological function or any disease or body condition that is associated with the isolated protein. Based solely on the fact that the protein was isolated from a cell membrane and it binds to protein X, applicant characterizes the isolated protein as receptor A. The function of protein X has also not been identified. The specification discloses a binding assay for determining other materials which bind to the receptor by adding the material to the complex of receptor A and protein X and determining the amount of inhibition of the binding of the complex as an indication that the material will bind to the receptor and thus be a therapeutic drug to effect control over the receptor. Also disclosed is the production of a monoclonal antibody that specifically binds to receptor A. There are no working examples using any materials to demonstrate such inhibition of binding, to assay the receptor or to identify any other material which binds to the receptor. The utility disclosed is for identifying materials that bind the receptor and the potential use of such materials as therapeutics.

Claims:

1. Isolated receptor A.
2. A method of identifying materials which bind to receptor A comprising:
a) forming a complex of receptor A and protein X in a liquid;
b) adding a material to be screened to said complex;
c) determining the amount of binding of said complex wherein an inhibition of said binding is an indication that said material binds to said receptor.
3. A monoclonal antibody which specifically binds to receptor A.

Analysis: The following analysis includes the questions that need to be asked according to the guidelines and the answers to those questions based on the above facts. For this fact situation, each claim will be analyzed separately.

Claim 1:

1) Based on the record, is there a "well established utility" for the claimed invention? The specification as filed does not disclose or provide any evidence that points to a property of the claimed receptor such that another non-asserted utility would be well established. Additionally, there is no art of record that discloses or provides any evidence that points to a property of the claimed receptor such that another non-asserted utility would be well established. Consequently, the answer to the question is no.

2) Has the applicant made any assertion of utility for the specifically claimed invention? Here, there is an asserted utility for the claimed invention. In fact, for claim 1 there are two asserted utilities, i.e., a) a method of identifying materials which bind to receptor A, and b) a method of making a monoclonal antibody.

3) Is the asserted utility specific? The answer to this question is yes. In this case, the method of identifying materials which bind to a specific receptor, namely receptor A and a method of making monoclonal antibodies to receptor A are methods that are not applicable to the general class of receptors. Therefore, there is an asserted specific utility for the claimed invention.

4) Is the asserted utility substantial? The answer to this question in each case is no. The method in 2a) above is a method of identifying those materials which bind to receptor A. Thus, to determine whether or not this method has a "substantial utility," it must be determined whether or not the material that binds to receptor A itself has a "specific and substantial utility." Here, the only utility asserted for the identified materials is a therapeutic to effect control over receptor A. Since neither the specification nor the art of record disclose any diseases or conditions associated with receptor A, a method of treating an unspecified, undisclosed disease or condition, does not define a "real world" context of use. Further research to identify or reasonably confirm a "real world" context of use is required. Since the asserted utility for the identified materials does not define a "real world" context of use, a method of identifying such materials also could not define a "real world" context of use.

The method in 2b) above is a method of making a material, i.e., a monoclonal antibody. Thus, to determine whether or not this method has a "substantial utility", it must be determined whether or not the monoclonal antibody itself has a "specific and substantial utility." Here, there is an asserted utility for the monoclonal antibody even though it is not explicit,

e.g., as a therapeutic drug to effect control over the receptor. However, since neither the specification nor the art of record disclose any diseases or conditions associated with receptor A, the asserted utility in this case essentially is a method of treating an unspecified, undisclosed disease or condition, which does not define a "real world" context of use. Treating an unspecified, undisclosed disease or condition clearly would require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. *See Brenner v. Manson*, 383 U.S. 519, 535–36, 148 USPQ 689, 696 (1966) (noting that "Congress intended that no patent be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use-testing", and stated, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.").
Since the asserted utility for the product (monoclonal antibody) does not define a "real world" context of use, a method of making such a product also could not define a "real world" context of use.
Thus, the conclusion from analysis is that both a 35 U.S.C. § 101 rejection and a 35 U.S.C. § 112, first paragraph, utility rejection should be made on claim 1.

Claim 2:
1) Based on the record, is there a "well established utility" for the claimed invention? Since the claim is directed to a specific method of use, the utility of this claim is limited to that use and the examiner should not look to a "well established utility" for the composition used in the claimed method. Consequently, there is no "well-established" utility for the method.
2) Has the applicant made any assertion of utility for the specifically claimed invention? Here, there is an asserted utility for the claimed invention, i.e., a method of identifying materials that bind to receptor A.
3) Is the asserted utility specific? The answer to this question is yes.
In this case, the method of identifying materials which bind to a specific receptor, namely receptor A, is a method that is not applicable to the general class of receptors. It is specific to receptor A. Therefore, there is an asserted specific utility for the claimed invention.
4) Is the asserted utility substantial? The answer to this question is no.
Specifically, the method essentially is a method of identifying a material, i.e., those materials which bind to receptor A. Thus, to determine whether or not this method has a "substantial utility", it must be determined whether or

not the material that binds to receptor A itself has a "substantial utility." Here, the only utility asserted for the identified materials is a therapeutic to effect control over receptor A. Since neither the specification nor the art of record disclose any diseases or conditions associated with receptor A, the asserted utility in this case essentially is a method of treating an unspecified, undisclosed disease or condition, which does not define a "real world" context of use. Treating an unspecified, undisclosed disease or condition clearly would require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. *See Brenner v. Manson*, 383 U.S. 519, 535–36, 148 USPQ 689, 696 (1966) (noting that "Congress intended that no patent be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use-testing", and stated, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.").

Since the asserted utility for the identified materials does not define a "real world" context of use, a method of identifying such materials also could not define a "real world" context of use.

Thus, the conclusion is that both a 35 U.S.C. § 101 rejection and a 35 U.S.C. § 112, first paragraph, utility rejection should be made on claim 2.

Claim 3:

1) Based on the record, is there a "well established utility" for the claimed invention? The specification as filed does not disclose or provide any evidence that points to a property of the claimed monoclonal antibody such that another non-asserted utility would be well established. Additionally, there is no art of record that discloses or provides any evidence that points to a property of the claimed monoclonal antibody such that another non-asserted utility would be well established. Consequently, the answer to the question is no.

2) Has applicant made any assertion of utility for the specifically claimed invention? Here, there is no explicitly asserted utility for the claimed monoclonal antibody. However, as stated in the analysis of claim 1 above, there is an implied asserted utility for the monoclonal antibody even though it is not explicit, e.g., as a therapeutic drug to effect control over the receptor.

3) Is the asserted utility specific? The answer to this question is yes. In this case, the monoclonal antibody is specific for a specific protein,

namely receptor A. Therefore, there is an asserted specific utility for the claimed invention.

4) Is the asserted utility substantial? The answer to this question is no. Specifically, since neither the specification nor the art of record disclose any diseases or conditions associated with receptor A, the asserted utility in this case is a method of treating an unspecified, undisclosed disease or condition, which does not define a "real world" context of use. Treating an unspecified, undisclosed disease or condition would require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. *See Brenner v. Manson*, 383 U.S. 519, 535–36, 148 USPQ 689, 696 (1966) (noting that "Congress intended that no patent be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use-testing", and stated, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.").

Thus, both a 35 U.S.C. § 101 rejection and a 35 U.S.C. § 112, first paragraph, utility rejection should be made on claim 3.

Caveat:

Let us assume for the moment that the specification also discloses that receptor A is present on the cell membranes of melanoma cells but not on the cell membranes of normal skin cells. Assume also that the examiner has found and made of record a journal article published prior to the application's filing date indicating that it is desirable to selectively detect melanoma cells as opposed to normal skin cells so as to diagnose that type of cancer. Does this change the above analysis?

For each of the claims, the above analysis changes right from the first question: Based on the record, is there a "well established utility" for the claimed invention? The answer to this question would change to yes in each case. Specifically, based on this record, there is a "well established utility" for the products of claims 1 and 3. The "well established utility" for the receptor A is a method of assaying for materials that bind to receptor A by contacting the materials to a complex of receptor A and protein X. Furthermore, making a monoclonal antibody to receptor A for diagnosing melanoma would constitute a well-established utility. Such utilities are "well established" because the disclosure of the properties of the receptor and antibody taken together with the knowledge of one skilled in the art indicates that these specific, substantial and credible utilities were known.

With respect to claim 2, since there is now evidence of record providing a

correlation between this method and diagnosing melanoma, i.e., materials identified by the method, such as the monoclonal antibody, can be used to diagnose melanoma, this method now has a "well established utility". Therefore, utility rejections under 35 U.S.C § 101 rejection and a 35 U.S.C. § 112, first paragraph, should not be made against claims 1-3.

ANNEX 2

Conserved Tryptophan and Proline in TM6

GPCR	TM6 as predicted by TMHMM
RUP35	AILFTITSIFATL**WAP**RIIMILY
GPR119	TVSVLIGSFALS**WTP**FLITGIVQ
ghrelin receptor	MLAVVVFAFILC**WLP**FHVGRYLF
CXCR3 chemokine receptor	LVVVVVVAFALC**WTP**YHLVV
5-hydroxytryptamine (serotonin) receptor 2A	LGIVFFLFVVM**WCP**FFITNIMAV
5-hydroxytryptamine (serotonin) receptor 2B	GIVFFLFLLM**WCP**FFITNITLVL
5-hydroxytryptamine (serotonin) receptor 2C	VLGIVFFVFLIM**WCP**FFITNILS
dopamine receptor D3	VAIVLGAFIVC**WLP**FFLTHVLNT
dopamine receptor D1	TLSVIMGVFVCC**WLP**FFILNCIL
histamine receptor H3	AVIVSIFGLC**WAP**YTLLMIIRAA
galanin receptor 1	TVLVVVVVFGIS**WLP**HHIIHLWA
neuropeptide Y receptor Y1	IMLLSIVVAFAVC**WLP**LTIFNTV
neurotensin receptor 1	VLRAVVIAFVVC**WLP**YHVRRLMF
melanocortin 4 receptor	ITLTILIGVFVVC**WAP**FFLHLIF
adenosine A1 receptor	LALILFLFALS**WLP**LHILNCITL
cannabinoid receptor 1	LVLILVVLIIC**WGP**LLAIMVYDV

ANNEX 3

A. TMHMM result

HELP with output formats

```
# Sequence Length: 353
# Sequence Number of predicted TMHs:  7
# Sequence Exp number of AAs in TMHs: 155.66569
# Sequence Exp number, first 60 AAs:  23.65865
# Sequence Total prob of N-in:        0.04392
# Sequence POSSIBLE N-term signal sequence
Sequence        TMHMM2.0        outside      1    29
Sequence        TMHMM2.0        TMhelix     30    52
Sequence        TMHMM2.0        inside      53    64
Sequence        TMHMM2.0        TMhelix     65    87
Sequence        TMHMM2.0        outside     88   106
Sequence        TMHMM2.0        TMhelix    107   129
Sequence        TMHMM2.0        inside     130   147
Sequence        TMHMM2.0        TMhelix    148   170
Sequence        TMHMM2.0        outside    171   184
Sequence        TMHMM2.0        TMhelix    185   207
Sequence        TMHMM2.0        inside     208   227
Sequence        TMHMM2.0        TMhelix    228   250
Sequence        TMHMM2.0        outside    251   264
Sequence        TMHMM2.0        TMhelix    265   287
Sequence        TMHMM2.0        inside     288   353
```

plot in postscript, script for making the plot in gnuplot, data for plot